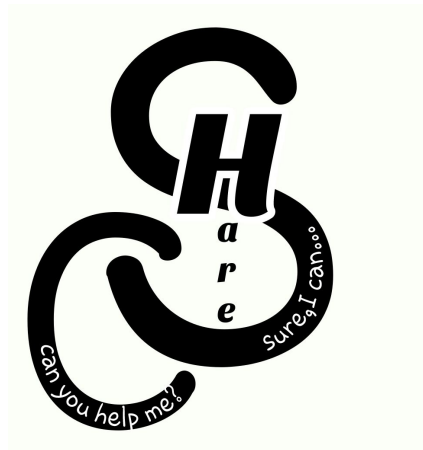




Regulation of ECF osmolarity and Na ions Concentration

- Regulation of extracellular fluid osmolality and sodium ions concentration is one of the kidney's functions. The amount of solutes that kidneys should excrete each day, containing: metabolic waste products, other excess ingested ions and other foreign substances and toxic substances, is 600mOsm. The human kidney can concentrate urine maximally to 1200mOsm/L. To know the minimal volume of urine that should excrete 600mOsm of solutes (waste products) and other substances, called obligatory urine volume, we use this equation:-

$$\frac{\text{solutes}}{\text{maximal urine conc.}} = \frac{600\text{mOsm/day}}{1200\text{mOsm/L}} = 0.5 \text{ L/day}$$

$$\frac{600 \text{ mOsm/day}}{1200 \text{ mOsm/L}} = 0.5 \text{ L/day}$$

- Sea water's NaCl (sodium chloride) concentration is high so it has high osmolarity (1200mOsm/L) and when a human drinks seawater, dehydration may occur. If someone drinks a liter of sea water, his body must excrete the excess amount of solutes in this water, in addition to the 600mOsm of solutes produced by his body. So, total amount of solutes equals 1800mOsm/L.

$$\text{Obligatory Urine Volume} = \frac{1800\text{mOsm/day}}{1200\text{mOsm/L}} = 1.5 \text{ L/day}$$

- So, the cause of dehydration is that if he drinks a liter of sea water, his body must excrete 1.5 liters of urine.
- Australian mouse's (an animal which lives in desert) maximal urine concentration can reach 10,000mOsm/L so if it drinks sea water, it'll not be affected. Its obligatory urine volume when it drinks a liter $= \frac{1200}{10000} = 0.12L = 120 \text{ ml}$. And since it lives in desert it can stay without water for long time and can take the amount of water that his body needs from water in food and by metabolism of food.

Regulation of water and electrolyte balance:-

- Daily intake of fluid should be matched with the output of water and electrolytes.
- **Daily fluid intake can be from:-**
 - Ingested fluids.
 - Water derived from food.
 - Water derived from food metabolism, especially carbohydrate.
- **Daily output of fluids:-**
 - Insensible water loss:
 - * Evaporation of water from respiratory passage ways.
 - * Diffusion of fluids through skin, which is minimized by cornified layer of skin. When someone is burned, dehydration happens, so he must ingest lots of fluids.
 - Through water sweat (sweating)

Note: diffusion through skin differs from sweating.
 - In stool.
 - In urine.

Regulation of ECF osmolarity:-

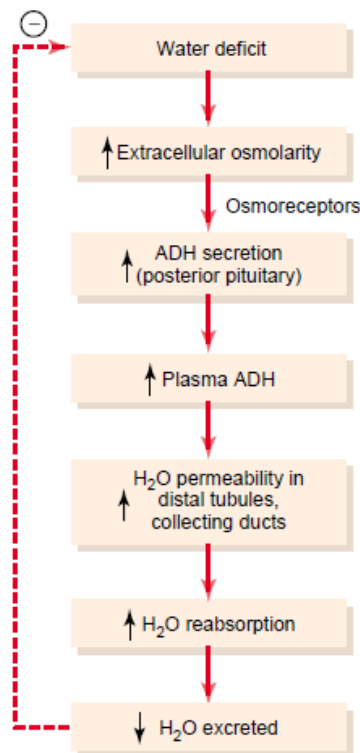


Figure 28-8

Osmoreceptor-antidiuretic hormone (ADH) feedback mechanism for regulating extracellular fluid osmolarity in response to a water deficit.

- When there is excess body water the osmolarity will decrease ▼, so kidneys must excrete large amount of urine that is diluted. And the opposite when the body water is deficient, osmolarity will increase▲, so kidneys decrease▼ urine excretion so osmolarity decrease▼ toward normal.
- The most abundant ions in the ECF are:-
 - Na^+ (sodium) = 142mOsm/L = 142mEq/L.
 - Cl^- (chloride) = 108 mOsm/L.
 - HCO_3^- (bicarbonate) = 24mOsm/L.

The negative ions (Cl^- , HCO_3^-) in the ECF are linked with Na^+ forming almost 94% of ECF's solutes, so we can consider them as the principle determinants of fluid movement through the cell membrane. The most important one is Na^+ , so when we speak about osmolarity of ECF, we are primarily speaking about Na^+ concentration.

Two mechanisms for regulation of ECF osmolarity:

- Osmoreceptor-ADH system.
- Thirst mechanism.

- **Osmoreceptor -ADH system:-**

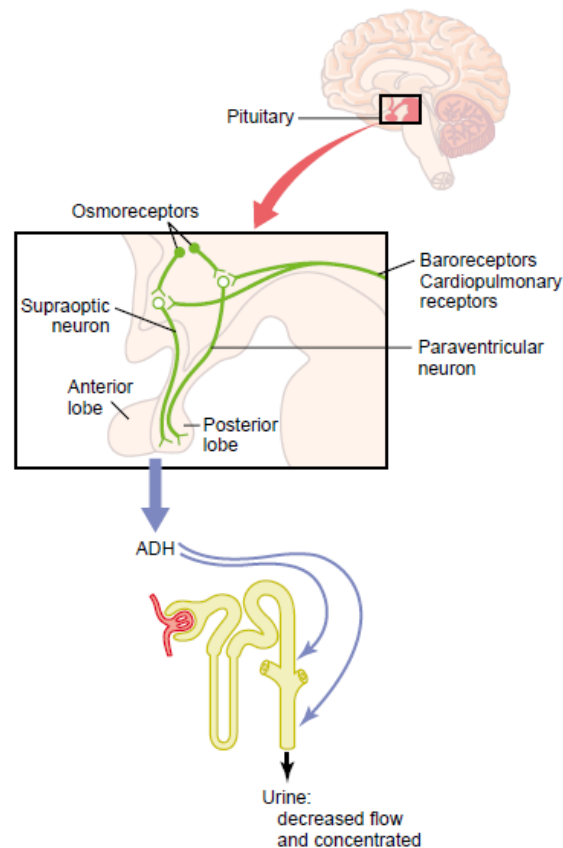


Figure 28-9

Neuroanatomy of the hypothalamus, where antidiuretic hormone (ADH) is synthesized, and the posterior pituitary gland, where ADH is released.

- ADH is secreted from posterior pituitary and formed in the hypothalamus. In hypothalamus, there are osmoreceptor cells which are special nerve cells.

When osmolarity increase▲ (of ECF), the osmoreceptor cells in the hypothalamus shrink, so send signals to other nuclei in the hypothalamus: supraoptic and paraventricular nuclei (cell bodies of this nuclei synthesize ADH, mainly supraoptic and to lesser extent the paraventricular cells). Then it is transported through the axons of these nuclei in vesicles or granules down to nerve ending of these nerve fibers which are located in the posterior

- pituitary gland.

When action potential reaches this nerve endings, ADH is released and absorbed by blood capillaries. Then it acts on renal tubules to increase $\blacktriangle$ reabsorption of water so decrease $\blacktriangledown$ osmolarity towards normal.

And when osmolarity of ECF decreases $\blacktriangledown$, the ADH decrease $\blacktriangledown$, so the water reabsorption decrease $\blacktriangledown$, so increase $\blacktriangle$ water excretion, so increase $\blacktriangle$ osmolarity to normal.

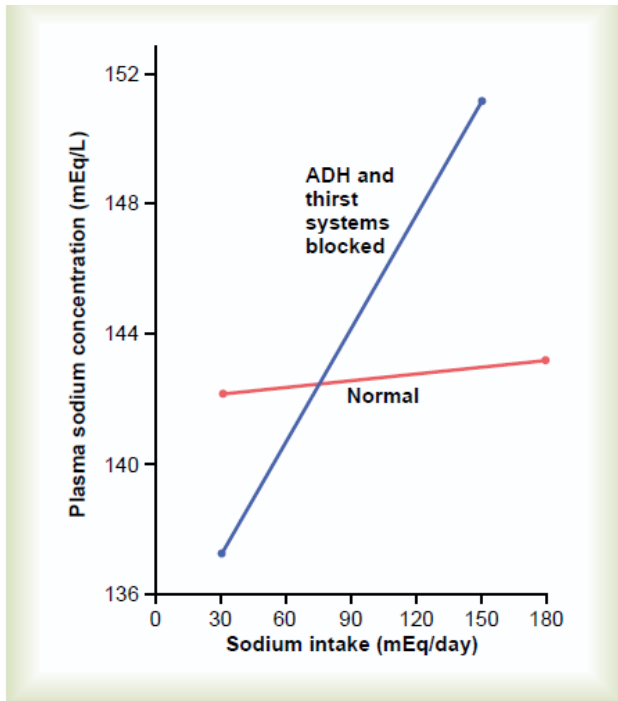


Figure 28-11

Effect of large changes in sodium intake on extracellular fluid sodium concentration in dogs under normal conditions (*red line*) and after the antidiuretic hormone (ADH) and thirst feedback systems had been blocked (*blue line*). Note that control of extracellular fluid sodium concentration is poor in the absence of these feedback systems. (Courtesy Dr. David B. Young.)

Line with red color, the increased $\blacktriangle$ sodium intake will not affect plasma sodium if there is normal osmoreceptor- ADH system.

Table 28–2**Regulation of ADH Secretion**

Increase ADH	Decrease ADH
↑ Plasma osmolarity ↓ Blood volume ↓ Blood pressure Nausea Hypoxia Drugs: Morphine Nicotine Cyclophosphamide	↓ Plasma osmolarity ↑ Blood volume ↑ Blood pressure Drugs: Alcohol Clonidine (antihypertensive drug) Haloperidol (dopamine blocker)

- The most important stimulus is increased ▲ osmolarity.
- Decreased ▼ blood volume (hypovolemia), due to haemorrhage, for example.
- Bleeding, vomiting and nausea.
- Alcohol causes Mac diuresis due to ADH inhibition.

Thirst mechanism:-

Table 28–3**Control of Thirst**

Increase Thirst	Decrease Thirst
↑ Osmolarity ↓ Blood volume ↓ Blood pressure ↑ Angiotensin Dryness of mouth	↓ Osmolarity ↑ Blood volume ↑ Blood pressure ↓ Angiotensin II Gastric distention

- The most important stimulus is ECF osmolarity.
- Angiotensin II is secreted during hypotension.
- Dryness of mouth and mucus membrane of oesophagus.
- Immediately after drinking water, the person feels partial or temporary relieve of thirst due to moisturizing of the mouth and oesophagus and gastric distension.

The point of this partial relieve, is to prevent excessive drinking and over hydration of the body fluids, because the body needs at least 30 to 60 minutes for water absorption from GIT and distribution through the body.

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